BIOENGINEERING, BIOINFORMATICS, AND ADVANCED TECHNOLOGIES

Bioengineering, bioinformatics, and other advanced technologies provide crosscutting tools that facilitate research in many disciplines. Bioengineering combines physics, chemistry, and mathematics, as well as basic engineering principles to enhance the study of biology, medicine, behavior, and health. Bioinformatics and computational biology apply computer science and advanced mathematics to the fields of biology and medicine to enable integration and analyses of biological, medical, behavioral, and health data. Other advanced technologies, such as biomedical imaging, proteomics, and genomics, facilitate characterization of complex biological processes.

The powerful tools and techniques of bioengineering, bioinformatics, and computational biology extend the capacity of science to perceive, capture, and manage information about biological processes. They have become integral components of NIAID-supported basic and clinical immunology research. Additional technologies, including proteomics, biosensor fabrication, biomedical imaging, and data integration, also are becoming important tools for researchers. Below are examples of NIAID-supported programs in these areas.

- **Mass spectrometry for high-throughput peptide characterization.** This program supports the development of chemical measurement instruments for the sequence analysis of peptide antigens presented in the major histocompatibility complex (MHC). The goal of this research is to develop a high-throughput method to study peptides that are recognized by the body as "self." Understanding how the immune system distinguishes between "self"—the body's own organs, tissues, and cells—and "not self"—foreign and potentially harmful agents—is relevant to all immune-mediated diseases.

- **Biodefense Proteomics Collaboratory.** This program supports research to dissect immune responses to viruses that are potential agents of bioterrorism, utilizing proteomics approaches to characterize dynamic changes in protein expression in inflammatory cells after pathogen exposure. This information will be compiled in a publicly available database. Bioinformatics approaches also will be used to correlate observed changes in protein expression with available data on changes in gene expression due to inflammation induced by viral infection or endotoxin shock.

- **Proteomics Research Centers: identifying targets for therapeutic interventions using proteomic technology**. The program will solicit proposals to identify proteins associated with the biology of microbes, host innate and adaptive immune response, and mechanisms of microbial pathogenesis. These projects will utilize and augment existing technologies or create novel proteomics approaches to perform early stage validation studies for identified proteins and cellular targets. To assist the centers, an Administrative Resource for Biodefense Proteomics Research Centers has been established. This resource will maintain a publicly available Web site that contains data and technology products generated by the Proteomics Research Centers. It will also monitor and facilitate the deposition of reagents and protein targets in a central repository. The Administrative Resource will coordinate programmatic meetings and the establishment of a scientific advisory board.

- **Systems approaches to innate immunity, inflammation, and sepsis.** This program supports research to create a comprehensive picture of innate immunity, the body's first line of defense against bacterial, viral, and fungal diseases. This multidisciplinary

systems biology approach will lead to an understanding of molecular-level innate immune responses triggered by bacterial and viral infections. One member of this team recently discovered a single protein that acts as a key switch point in innate immune responses to both bacterial and viral infections. In determining how this protein functions, the team of scientists learned why certain symptoms, such as fever, occur regardless of the cause of infection.[22]

- **Modular gene assembly.** Researchers are developing a new system for engineering genes on the basis of their binding and activation properties. This technology will enable the formation, selection, and assembly of genes based on individual functional traits, which could lead to the development of novel therapeutic compounds such as custom antibodies and immunosuppressants.

- **Microchip drug delivery system.** This program supports development of a novel drug delivery device that uses silicon-based microchips to deliver complex regimens of bioactive agents to specific organs or tissues. Researchers have demonstrated that a silicon-based microchip device with no moving parts can be operated *in vivo*. This device will allow for controlled delivery of a concentrated amount of drugs or bioactive compounds to affected tissue and has the advantage of eliminating possible toxic side effects and inefficient delivery of systemically administered compounds.

- **Alliance for Cellular Signaling (AfCS).** AfCS is a large-scale collaborative program co-funded by the National Institute of General Medical Sciences (NIGMS), NIAID, the National Cancer Institute, several pharmaceutical companies, and private sources. The primary goal of the AfCS is to dissect signaling pathways in mammalian cells in order to understand how cells interpret and respond to external signals. All of the materials and information developed through the AfCS are freely available to the biomedical community worldwide. More information is available at *www.signaling-gateway.org*.

- **NIGMS Protein Structure Initiative.** NIAID contributes to the support of this NIGMS-sponsored program to determine the structure of proteins from the genomes of pathogenic protozoans and malaria parasites. The program involves computer prediction of protein domains for target selection, high-throughput protein expression, crystallization, and structural analysis. More information is available at *http://www.nigms.nih.gov/psi/*.

- **Whole-organism imaging of immune response.** This program uses imaging technologies to detect the accumulation of labeled T cells and macrophages in organ transplants and to examine the development of systemic autoimmunity *in vivo*. The ability to monitor T cell migration to and accumulation in organs such as the liver, kidney, and bowel, or in the central nervous system is important to understanding immune responses to pathogens and immune-mediated diseases. Another NIAID-funded project is developing new magnetic resonance imaging contrast reagents (dyes) to track immune responses *in vivo*.

- **Genomic databases and analysis tools.** NIAID supports databases of genomic information and analysis tools for the multidisciplinary study of sexually transmitted pathogens, including pneumoniae, chlamydia, papillomavirus, herpes, and gonorrheae. These tools, which include dynamic graphics and Web-based data mining and sequence analysis tools, extend beyond molecular sequence data. This resource is available from the Los Alamos National Laboratory and is also supported by the U.S. Department of Defense. See *www.stdgen.lanl.gov* for more information.

- **Bioinformatics Integration Support Contract (BISC).** The goal of BISC is to advance the discovery and testing of new therapies for immune-mediated diseases and to further understanding of the basis of innate and adaptive immunity by providing advanced computer support for scientific data handling and disseminating best practices in scientific data analysis. BISC will provide the means for scientists to easily access, generate, analyze, and exchange complex high-quality datasets. Specifically, BISC will provide a data repository, a suite of bioinformatics analysis tools, a suite of data integration tools, consulting advice on technical and data management issues, and an archive facility to scientific researchers funded by the NIAID Division of Allergy, Immunology, and Transplantation and the National Institute of Diabetes and Digestive and Kidney Diseases.

- **HIV Database and Analysis Unit.** This unit includes the HIV Genetic Sequence Database and the HIV Molecular Immunology Database. The Genetic Sequence Database compiles sequence information from GenBank and other international databases and then conducts indepth analyses of HIV genomes. The Molecular Immunology Database compiles all published immunologic information on humoral and cellular immune epitopes from HIV proteins. These databases also provide analysis tools to the user community at *http://hiv-web.lanl.gov* and *http://hiv-web.lanl.gov/immunology/index.html*.

- **Immune epitope database and analysis program.** The primary goals of this program are to develop and maintain an integrated, Web-based, searchable database of antibody binding sites (antibody epitopes) and antigenic MHC-binding peptides (T cell epitopes) for a wide variety of infectious agents and immune-mediated diseases, with emphasis on category A, B, and C bioterrorism agents as well as emerging and re-emerging infectious diseases. It is anticipated that the information contained within the database and the availability of analysis tools will facilitate identification of novel vaccine candidates and immunotherapeutic strategies to improve biodefense strategies. HIV epitopes are excluded; those data are already catalogued in the HIV Molecular Immunology Database at Los Alamos Laboratory.

- **Innovations in Biomedical Computational Science and Technology.** This trans-NIH program announcement was developed in response to a report by the NIH Working Group on Biomedical Computing. The report noted the continued need to improve the interface between biomedical research and biomedical information science and technology. This program promotes research and development in database design, graphical interfaces, query approaches, data retrieval, visualization, integration, and manipulation.